TOLERANCE OF ANIMALS TO HYPEROXIA, HYPERCAPNIA AND HIGH TEMPERATURE AFTER ADAPTATION TO LOWERED BAROMETRIC PRESSURE.

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ABSTRACT: This research was conducted on white mice. The tolerance of the animals was studied according to their survival in conditions of a gaseous atmosphere containing 96% oxygen with an elevated amount of CO_2 (40%) and high temperature (50-60%) before and after adaptation to conditions of lowered barometric pressure.

It was established that adaptation to hypoxia will not result in an increase in the tolerance of animals to the effect of hyperoxia and high CO_2 concentration in the inhaled air. The tolerance to high temperature in the adapted animals increases slightly.

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In studying the process of adaptation hypoxia many investigators have paid basic attention to the effects which indicate a nonspecific increase in the tolerance of the adapted animals to different adverse influences [1,2].

By developing this point of view several authors [1,2] assumed that adaptation to hypoxia in essence must be accompanied by an increase in the tolerance of the adapted animals to practically any adverse environmental factor.

At the same time analysis of changes which occur with the development of adaptation to hypoxia shows that the majority of reactions which determine the restructuring of the organism have a rather specific character. They are directed toward an increase in the oxygen transport to the tissues and to the cellular structures of the brain which are especially sensitive to oxygen deficiency. Thus the works of P. Ber, I. M. Sechnov, D. Barcroft, Holden, Hurtado and others [3, 4, 8, 9, 12] established that an increase in the minute volume of pulmonary ventilation, the oxygen capacity of the blood and an increase in the blood flow through the lungs, heart and brain is one of the important adaptation reactions with hypoxic hypoxia.

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In this respect there arises the question as to whether the adaptation to hypoxic hypoxia can be accompanied by less in the tolerance of animals to the effect of certain adverse environmental factors, the adaptation to which produces a restructuring of the organism in its character that is opposite to that observed

with hypoxia. To study this problem we made an investigation of the tolerance of animals adapted to hypoxia to such influences as increased oxygen content in the inhaled air (95%), increased amount of carbon dioxide (up to 40%) and high temperature of the environment (+60°C).

The adaptation reactions which arise with oxygen deficiency are opposite those which occur under the effect of an oxygen excess.

We can judge this on the basis that an increased amount of oxygen in the inhaled air in man and animals produces a decrease in the ventilation of the lungs [7, 11], a decrease in the number of heart contractions (6, 10), a drop in the amount of hemoglobin and the number of erythrocytes in the peripheral blood. These reactions are opposite those which occur with hypoxia and are directed to guarding the organism from an increased amount of oxygen. Hence it is of interest to study the changes in the tolerance of an organism to acute hypoxia after a prolonged effect of hyperoxia.

On the other hand A. G. Zhironkin [5] established the possibility of increasing the tolerance of animals to the toxic effect of high oxygen pressures by preliminary conditioning them to oxygen deficiency. As one of the probably mechanisms of adaptation the author assumes that the hyperoxia of tissues on this basis is "hyperoxic hypoxia" and the effect of hypoxic conditioning is specific and directed to the adaptation to different forms of hypoxia including the "hyperoxic".

Consequently, it is necessary to explain if the adaptation of the organism to hyperoxia occurs in general and if the change in tolerance to hyperoxia occurs following prolonged high-altitude and pressure-chamber adaptation.

With adaptation to hypoxic hypoxia there is developed a hyperventilation as a result of which the tissues which undergo oxygen deficiency are simultaneously located in a state of hypocapnia. Here there is a basis for assuming that the tolerance of animals to high concentrations of CO_2 in the inhaled air may be lowered.

In the process of adaptation to hypoxia an essential role is played by the restructuring of the blood circulation, in particular the redistribution of the blood stream, increase in the blood stream through the brain, lungs and heart and a respective decrease in the blood stream through the skin, muscles and internal organs. With an increase in temperature of the atmosphere the adaptative reactions of the blood circulation have to a significant degree an /74
opposite character.

In our experiments we set the purpose of explaining the change in the tolerance of an organism to the following adverse factors:

To hyperoxia after high-altitude and pressure-chamber adaptation;

To an increased concentration of carbon dioxide in a gaseous atmosphere;

To elevated temperatures;

To acute hypoxia after prolonged effect of hyperoxia.

The investigations were carried out on white mice. Experiments with hyperoxia were set up in a chamber especially prepared of organic glass which guaranteed visual observation of the animals with retention of a constant gaseous atmosphere.

Ventilation of the chamber with pure oxygen or with a mixture with nitrogen was carried out from high-pressure tanks. Through the reductors with a course and fine regulation, the gases were admitted through the hose with a calibrated rheometer and then to the gas mixer and into the chamber.

Humidity and carbon dioxide were removed from the chamber by ventilation. Furthermore, during the day a small pump was turned on which circulated the "air" of the chamber through chemical absorbents of carbon dioxide and moisture.

Feed, bedding and other objects were placed into the chamber through a receiver-transmitter hatch which was hermetically sealed. All manipulations in the chamber were carried out using rubber gloves with long hands that were attached to the projection of the openings on the sides of the walls. Removals from the chamber were made every day. The gas composition of the chamber was controlled on an Ors and "Khelige" gas analyzer.

Adaptation of the animals was carried out in mountains at altitudes of 2000 m (Terskol) for a period of 16 days and at an altitude of 3800 m (Ledovaya Baza) for 14 days. Interrupted adaptation in the pressure chamber was accomplished by daily ascents for a period of 13 days to ever-increasing altitudes up to 7000 m.

In the first series of experiments we determined the lifetime of the mice at an "altitude" of 9000 m following introduction of 90-92% oxygen for a period of 2, 3 and 4 days.

The experimental results showed that the tolerance of the animals to acute oxygen starvation is decreased, this being to a larger degree as the duration of priming with oxygen is increased. The difference in the altitude tolerance of the control mice and the experimental mice is especially pronounced during the first minutes of the effect of hypoxia. In proportion to their residence at high altitudes this difference was gradually smoothed out (Fig. 1).

The basic reason for lowering the tolerance of an organism to acute hypoxia is apparently disruption in the gaseous metabolism produced by damage to the lungs which develops under the effect of hyperoxia. In this respect we set up one more experiment on determing tolerance to acute oxygen starvation following the effect of /75 lower (subtoxic) concentrations of oxygen.

The mice (11 in number) were kept for 2.5 days in a gaseous environment consisting of 40 and 60% oxygen with a mixture of nitrogen. Then along with the control animals they were subjected to ascent in a pressure chamber to altitudes of 9000 and 10,000 m Exposure at each altitude was 10 minutes.

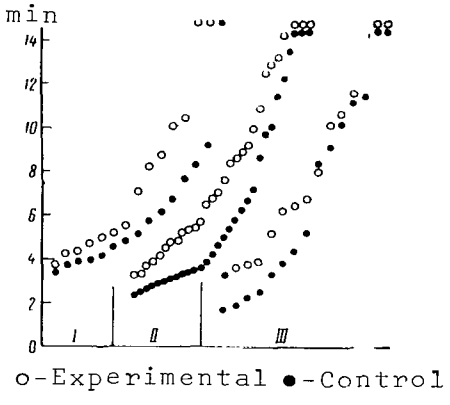

Fig. 1. Lifetime of the Mice at an "Altitude" of 9000 m Following Two (I), Three (II) and Four (III) Days of Residence in an Atmosphere of Pure Oxygen.

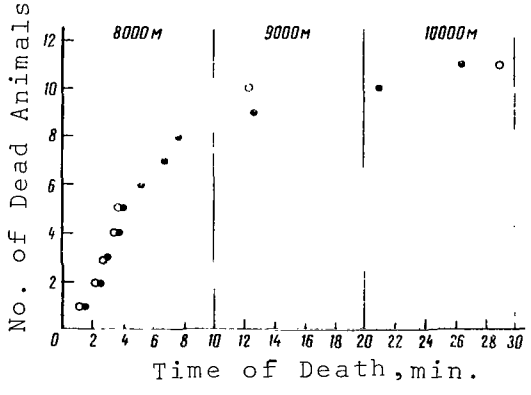

Fig. 2. Changes in the Tolerance of Mice to Acute Hypoxia After Residence in a Hyperoxic Gaseous Medium.

The average lifetime at "high altitude" of the mice who have previously been exposed to a hyperoxic gaseous medium was 8 min 30 sec and the control animals was 6 min., 36 sec. (Fig. 2).

By comparing the results of these two experiments we can come to the conclusion that the toxic concentrations of oxygen decrease /76 but the nontoxic probably increase slightly the tolerance of animals to acute hypoxia.

The second series of experiments was carried out to determine

the survival of animals in an atmosphere of pure oxygen after high altitude and interrupted pressure-chamber adaptation.

The results of the first two experiments of this series showed that in a hyperoxic atmosphere the animals who were acclimatized at "Ledovyaya Baza" died somewhat earlier than those from "Terskol". However, on the 5-6th days of priming this difference disappeared and all the animals died almost simultaneously (Table 1).

TABLE 1. SURVIVAL OF MICE IN AN ATMOSPHERE OF PURE OXYGEN ON THE THIRD (I) AND NINTH (II) DAYS FOLLOWING HIGH-ALTITUDE ADAPTATION

Group *	on 4th day	on 5th day	on 6th day	Group *	on 4th day	on 5th day	on 6th day
I				II			
"Ledovaya"	2	5	3	"Ledovaya"	2	4	4
"Terskol"	3	4	3	"Terskol"	-	5	5
Control	1	5	4	Control	-	3	7

*Each group has 10 animals.

Under analogous conditions we carried out two experiments on mice following interrupted pressure-chamber adaptation. No substantial statistically meaningful distinctions in change of tole rance of the animals to hyperoxia appeared here.

Thus the adaptation reactions which arise with adaptation of the organism to oxygen deficiency not only do not protect but to some degree even facilitate in several of the animals an earlier development of the pathological process which is produced by the toxic effect of pure oxygen.

In the third series of experiments we determined the tolerance of mice to high concentrations of carbon dioxide in a mixture with oxygen following pressure-chamber and high-altitude adaptation.

The first experiment was set up on 10 mice on the second day after cessation of the interrupted pressure-chamber adaptation (carried out in the period from the 8th to the 22nd of December, 1964) and on 10 control animals. In the chamber we created a stream of a gaseous mixture, 1.2 liters/min in volume enriched with CO_2.

The average lifetime of the mice in this gaseous atmosphere was: The adapted animals 171 min (a range from 43 to 282 min) and the control animals 156 min (from 69- 282 min).

The second experiment was carried out on 15 mice on the 8th day following a month high-altitude adaptation and on 15 control animals. The stream of the gaseous mixture was created the same but the carbon dioxide content in the first three hours was increased from 27 to 43% after which it remained constant. /77

The average lifetime of the mice "acclimatized" in mountains was 300 minutes (from 208 to 373 min) and the control animals 296 minutes (from 210 to 363).

In spite of the fact that the overall lifetime of the mice in the first and second experiments was different (in connection with a nonidentical percentage content of carbon dioxide in the gaseous atmosphere of the chamber), the time of death of the experimental and the control mice was practically the same. In the fourth series of experiments we determined the effect of pressure-chamber and high-altitude adaptation on the tolerance of animals to elevated temperature.

The first 2 experiments were carried out at a temperature of the surrounding atmosphere of 60° C every 1-2 days following a single and a three-time interrupted adaptation of the mice in the pressure chamber.

In these experiments the mice who were adapted to high altitudes (especially following a three-time repetition of adaptation) were found to be more tolerant of high temperatures than were the control animals (Table 2).

TABLE 2. THE EFFECT OF INTERRUPTED PRESSURE-CHAMBER ADAPTATION ON THE SURVIVAL OF MICE AT A TEMPERATURE OF 60°

Group	No. of Animals	Time of Death, Min.				
		10	20	30	40	50
After first adaptation	20	2	9	6	3	-
After third adaptation	20	-	6	9	3	2
Control	20	5	14	1	-	-

The third experiment was set up at a temperature of 50 ± 2° after 5-8 days following a month's adaptation of mice at high altitudes (Fig. 3). In these less strict temperature conditions the average lifetime of the mice adapted to high altitude was 58 minutes, 2 seconds, and the control animals was 31 minutes, 43 seconds, i.e., a high tolerance to elevated temperature was observed in the animals adapted to hypoxia.

By estimating the results of all the series of experiments it follows first of all to note that adaptation to hypoxia does not

lead to an increase in the tolerance of animals to the effect of hypoxia and a high concentration of CO_2 in the inhaled air.

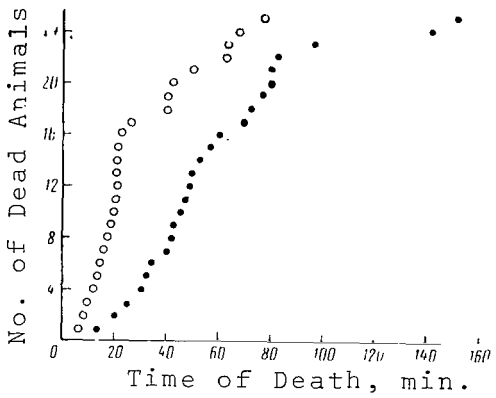

Fig. 3. Survival of Mice at a Temperature of 50 ± 2° C. Designations are the Same As in Figure 1.

If the criterion of tolerance is assumed to be the survival of the animals under changed conditions, then it is correct to assume that the practically identical lifetime of the control animals and those adapted to hypoxia in a gaseous environment, enriched with oxygen and carbon dioxide indicates a slight decrease in the tolerance of the adapted animals to these factors. Such a conclusion is based on the fact that the agonic phase during the time of which there appeared acute hypoxia is found to be more lengthy in the adapted animals. As a result of this the time of survival in the control animals and the experimental animals is practically the same, however, the time of retention of a relatively high functional level under these influences in the experimental animals as a rule is somewhat shorter than in the intact animals. Thus the results of the work indicates that a nonspecific increase in the tolerance of the animals who were adapted to hypoxia to noxious factors does not appear in all cases. It is missing when the damaging effect leads to the development of adaptational specific reactions having an opposite direction to the adaptive reactions developing during hypoxia. /78

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